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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
09/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@choate.com

Office Action Summary	Application No.	Applicant(s)	
	10/570,556	DANISHEFSKY ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *5,6,24,26,28-34 and 36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-23,25,27 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

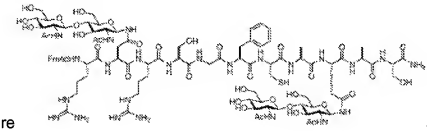
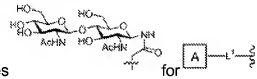
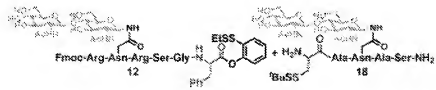
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on June 2, 2008 is acknowledged. Claim 40 has been cancelled. Claims 1-39 are pending in this application.

Restriction

1. Applicant's election with traverse of Group I and elected the polyfunctionalized peptide of structure  and the species  for , and for peptide acyl donor and peptide amino acceptor, applicant elects 

, and for an immunogenic carrier, applicant elects Keyhole Limpet Hemocyanin (KLH) in the reply filed on June 2, 2008 is acknowledged. Applicant indicates that the elected species read on claims 1-4, 7-23, 25 and 27. The traversal is on the ground(s) that the present claims are drawn to a method of native chemical ligation of two functionalized peptides, wherein the peptide amino acceptor comprises an N-terminal cysteine residue. A single

general inventive concept linking the polyfunctionalized peptides of Groups 1, 2, 3, 4 and 5 is that they may each be prepared by a general method, and the common feature of the polyfunctionalized peptides is that they all comprise a cysteine residue at the point of ligation. Furthermore, Applicant argues that the same two amino acids were joined via ligation (i.e., peptide acyl donor = F, peptide amine receptor = C). Applicant argues that it would not be an undue burden on the Examiner to search and examine these groups simultaneously. This is not found persuasive because the polyfunctionalized peptides produced are patentably independent and distinct peptides since the structures are different. Furthermore, the sequences of SEQ ID NOS: 6-8 are patentably independent and distinct from each other. Further, the reagents such as peptide acyl donor and peptide amine receptor involved in the methods are structurally different for each invention. Therefore, there is lack of unity and each polyfunctionalized polypeptide is an independent invention.

The requirement is still deemed proper and is therefore made FINAL. Claims 5-6, 24, 26, 28-34 and 36-39 are withdrawn from further consideration as being drawn to nonelected species and invention, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. The polyfunctionalized peptide of claim 35 appears to be free of prior art. Search was extended to the broad Markush of claim 1, and prior art was found. Claims 1-4, 7-23, 25, 27 and 35 are examined on the merits in this office action.

Objection

2. The specification is objected to for the following: The specification indicates "incorporation by reference" of certain documents. The MPEP states the following: "An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference. An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, >or< (2) a U.S. patent application publication, **>which patent or patent application publication does not itself incorporate such essential material by reference..."Essential material" is defined in >37CFR1.57(c)< as that which is necessary to (1) **>provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112..." (see MPEP 608.01(p)).

Rejection

35 U.S.C. 112, 2nd

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-4, 7-21, 23, 25, 27 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

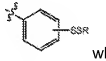
5. Claim 1 recites, "...under suitable conditions to effect ligation". It is unclear what conditions are encompassed with the suitable conditions to effect ligation. For example, it is unclear if the temperature, the time, the buffer conditions, reagent and others effect ligation. Because claims 2-4, 7-21, 23, 25 and 27 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

6. Claim 1 recites, "...wherein two or more non-adjacent amino acids are independently substituted with a moiety having the structure: with the proviso that the peptide sequence between any two consecutive, non-adjacent, amino acids bearing A-L^1-moiety comprises at least one cysteine residue". By looking at the elected species and invention of claim 35, it is unclear what is meant by two consecutive, non-adjacent amino acids bearing A-L^1-moiety. The species of claim 35 has 4 consecutive amino acids between the amino acids bearing A-L^1-moieties. Because claims 2-4, 7-23, 25, 27 and 35 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

7. Claim 1 recites, "R^{X0} is a group such that the moiety $-C(=O)OR^{X0}$ can be made to undergo ligation with the peptide amino acceptor..." It is unclear what R^{X0} is since it seems to be referring back to the moiety $-C(=O)OR^{X0}$ also has the variable R^{X0}. Claims

2-4, 7-15, 20-23, 25, 27 and 35 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

8. Claim 7 recites, "The method of claim 1, wherein each occurrence of A, A1 and A2 is independently selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, STN, (2,3)ST, Le^y, Le^x, N3, Tn, 2,6-Stn, Gb3 and TF." It is unclear what KH-1, STN, (2,3)ST, Le^y, Le^x, N3, Tn, 2,6-Stn, Gb3 and TF stand for and what these encompass. For example, according to NCBI, TF stands for transferrin (AAB35968), tissue factor (AAB20755), turmolytic factor (AAB47040), TF protein (AAH20671); N3 stands for N3 protein (ABT17358), sperm protein associated with the nucleus on the X chromosome N3 (Q0ZNK1), etc. The specification does not define what these compounds are. They appear not to be commonly known in the art.

9. Claims 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 recites, "the method of claim 9, wherein R^{X0} has the structure  wherein R is an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety. It is unclear what "SS" is, since it is not defined in the claims. Since claims 18-19 depend on indefinite claim 17 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

35 U.S.C. 112, 1st

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-3, 8-23, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a method for preparing a polyfunctionalized peptide comprising a peptidic backbone made up of four or more

amino acids wherein two or more non-adjacent amino acids are independently substituted with an A-L^1-moiety…each occurrence of A, A_1 and A_2 is independently an aliphatic, heteroaliphatic, aromatic, heteroaromatic, aryl, heteroaryl or a pharmaceutically useful group or entity. The generic statements aliphatic, heteroaliphatic, aromatic, heteroaromatic, aryl, heteroaryl or a pharmaceutically useful group or entity do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 1-3, 8-9 and 21-23 are broad generics with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of compounds, any aliphatic, heteroaliphatic, aromatic, heteroaromatic, aryl, heteroaryl, any class of biologically active compounds that are pharmaceutically useful, any class of peptide or a peptide-like molecule that are biologically active and are pharmaceutically active and useful, and any small or macromolecules that have biological functions. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a

correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules that can be peptide linked having pharmaceutical function, and other synthetic peptide or peptide-like molecule, peptidomimetics, amino acid mimetics and other small and macromolecules having pharmaceutical activity.

The specification discloses that "the term pharmaceutically useful group or entity refers to a compound or fragment thereof, or an organic moiety which, when covalently attached to a peptide or protein, can exert some biological or diagnostic function or activity when administered to a subject, or enhance the therapeutic, diagnostic or preventive properties of the parent peptide and/or protein in biomedical applications…pharmacokinetics modifiers can include, for example, antibodies, antigens, receptor ligand, hydrophilic, hydrophobic or charged groups. Biologically active modifiers include, for example, therapeutic drugs and prodrugs, antigens, immunomodulators…" (see paragraph [0077] of instant specification 2007/0173636 A1). The specification discloses that "the term biolmolecules" refers to molecules (e.g., proteins, amino acids, peptides, polynucleotides, nucleotides, carbohydrates, sugars, lipids, nucleoproteins, glycoproteins, lipoproteins, steroids, etc) which belong to classes of chemical compounds that are commonly found in cells and tissues…enzymes,

receptors, neurotransmitters, hormones, cytokines, cell response modifiers such as growth factors and chemotactic factors, antibodies, vaccines, haptens, toxins, interferons, ribozymes, anti-sense agents, plasmids, DNA and RNA (see paragraph [0078] of instant specification as above). Further, the specification discloses that "the term small molecule refers to molecules whether naturally-occurring or artificially created that have a relatively low molecular weight…they produce a local or systemic effect in animals, preferably mammals, more preferably humans…less than about 1500 g/mol" (see paragraph [0079] of instant specification above). Classes of small molecule drugs are disclosed in instant paragraph [0080]. These compounds, such as anti-AIDS substances, anti-cancer substances, antibiotics, lubricants, etc are genus of compounds described only in its function. The specification discloses that "the term macromolecules refers to molecules whether naturally occurring or artificially created that have a relative high molecular weight, generally above 1500 g/mole. Examples of macromolecules include proteins, enzymes, growth factors, cytokines, peptides, polypeptides, polylysine, proteins, lipids, polyelectrolytes, immunoglobulins, DNA, RAN, ribozymes, plasmids, and lectins (see paragraph [0082]). Instant paragraph [0083] discloses that examples of diagnostic labels include labels that can be used in medical diagnostic procedures, such as radiopharmaceutical or radioactive isotopes for gamma scintigraphy and positron emission tomography (PET), MRI, etc.

The specification discloses that "the term aliphatic includes both saturated and unsaturated, straight chain or branched aliphatic hydrocarbons, which are optionally substituted with one or more functional groups (see instant paragraph [0051]). Preferred

embodiments are listed in instant paragraph [0052]. The specification discloses that "heteroaliphatic refers to aliphatic moieties in which one or more carbon atoms in the main chain have been substituted with a heteroatom (see instant paragraph [0055]). Instant paragraph [0058] discloses that "the term aromatic moiety refers to stable substituted or unsubstituted unsaturated mono- or polycyclic hydrocarbon moieties having preferably 3-14 carbon atoms; Heteroaromatic moiety refers to stable substituted or unsubstituted unsaturated mono-heterocylic or polyhetereocyclic moieties having preferably 3-14 carbon atoms (see instant paragraph [0059]). The instant paragraph [0062] discloses that "the term heteroaryl refers to heteroaromatic moieties excluding those attached via an aliphatic or heteroaliphatic moiety.

The working examples describe glycan conjugated peptides being chemically ligated together (see Schemes 1-2 and 5-11). The specification does not describe any other A, A1, and A2 that are aliphatic, heteroaliphatic, aromatic, heteroaromatic, aryl, heteroaryl or a pharmaceutically useful group or entity, such as synthetic polymers comprising repeating polypeptide units or any other proteins, a polymer of PEG that increases the serum half-life, or any other type of peptide or peptide-like molecule or compounds that act are aliphatic, heteroalipatic, aromatic, heteroaromatic, aryl heteroaryl or pharmaceutically active. Description of glycans, oligosaccharides is not sufficient to encompass numerous other pharmaceutically useful group that belongs to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. In case of peptide or protein, the number of possible sequences a peptide or protein compounds

having a pharmaceutical activity is vast. For example, for a GLP-2 peptide having a 33 amino acid residues, there are $33^{20} = 2.35 \times 10^{30}$ different possibilities including variances and derivatives that have pharmaceutical activity. There are also varying sizes and varying compositions that make up the genus of aliphatic, heteroaliphatic, aromatic, heteroaromatic, aryl, and heteroaryl groups. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

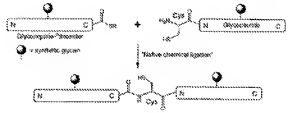
The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

35 U.S.C. 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bertozzi et al (Science, 23 March 2001, 291: 2357-2364, filed with IDS).

14. Bertozzi et al teach glycoprotein synthesis by convergent coupling of glycopeptides fragments, 

. Assembly from synthetic glycopeptides fragments using the technique of native chemical ligation. Bertozzi teaches that one fragment is functionalized as a COOH-terminal thioester, and the other bears an NH_2-terminal cysteine residue. A transthioesterification reaction between the two components produces an intermediate thioester that rearranges to the peptide bond shown in the product (see Figure 3(B), p. 2359). Since glycans are pharmaceutically useful group (as disclosed in the specification, see paragraph [07078]), this meets the limitation of claims 1-4 and 8.

35 U.S.C. 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

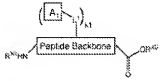
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

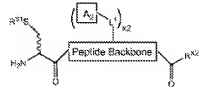
18. Claims 1-4, 8-15, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hojo et al (Tetrahedron Letters, 2003, 44: 2961-2964, filed with IDS) in view of Miller et al (Angewandte, Jan. 27, 2003, 42(4): 431-434, filed with IDS).

19. Hojo et al teach the preparation of peptide thioester carrying N-linked core pentasaccharide by the Fmoc solid phase method with a combination of the benzyl-protection strategy at the carbohydrate portion (see abstract). Hojo teaches the structure of extracellular Ig domain of emmprin carrying pentasaccharide unit 1 (see Figure 1, p. 2961). Hojo teaches that if the glycosylated peptide thioester can be

prepared, these methods can be directly applied to the glycoprotein synthesis (see p. 2961, right column). Figure 2 teaches the synthetic procedure of the N-terminal peptide thioester carrying pentasaccharide unit 4 (see p. 2962, right column). Synthetic procedure of the Ig domain (34-94) chemically ligated is taught in Figure 4 (see p. 2963). According to Figure 1, there is at least one cysteine residue between the A-L^1 moieties. Hojo teaches that the N-linked glycopeptides is at the N-terminal end of the Ig domain (34-58) (see Figure 4). The difference between the reference and the instant claims is that the reference does not teach reacting a peptide acyl donor comprising a peptidic backbone made of two or more amino acids wherein said peptide acyl donor



has the structure and with a peptide amino acceptor having the



structure .

20. However, Miller et al teach synthetic N-linked glycoprotein synthesis. Miller teaches building a complex glycodomain and incorporating it into a polypeptide setting, and how the pieces of the puzzle can be interfaced (see p. 432, left column, 1st paragraph). Miller teaches natural O- and N-linkages as opposed to non-natural arrangements…and there is no limit to the structural complexity of the carbohydrate sectors of the glycopeptide targets (see p. 432, left column, 2nd paragraph). Scheme 1 teaches the convergent approach to N-linked glycopeptides using Fmoc synthesis.

Scheme 2 teaches the glycan preparation and peptide conjugation. The peptide is Fmoc protected at the N-terminal end and the glycan is conjugated onto the Asn residue of the peptide (see Scheme 2). Scheme 4 teaches the chemical ligation of an N-linked glycopeptides with peptide (see Scheme 4 and p. 433, left column, 2nd full paragraph). Miller teaches in Scheme 4 that ligation was in the presence of PBS and excess sulfanylethane-2-sulfonate (sodium 2-mercaptoethanesulfonate), which is same as the 2-mercaptoethanesulfonic acid. Scheme 5 teaches native chemical ligation of a pentasaccharide glycopeptides and a pentadecapeptide (see Scheme 5 and p. 433, right column, 1st paragraph). Schemes 1-2, 4 and 5 teach that StBu protects the functional group of the cysteine residue. Miller teaches that the N-linked glycopeptide is at the C-terminal end of the pentadecapeptide (see Schemes 4 and 5).

21. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Hojo et al and Miller et al to produce a polyfunctionalize peptide having multiple N- or O-glycosylated peptides. One of ordinary skill in the art would have been motivated to combine the teachings, since Hojo teaches the method of making a pentasaccharide glycosylated peptide sequence by chemical ligation of two peptide sequences (one that is N-linked glycosylated, and one that is not), and Miller teaches pentasaccharide glycosylated peptide sequence by chemical ligation of two peptide sequences (one that is N-linked glycosylated, and one that is not). Both references teach the importance of glycosylation in a wide range of biological processes. There is a reasonable expectation of success, both teach the pentasaccharide glycopeptide that is glycosylated at the Asn residue. Hojo teaches

chemical ligation of an Asn-glycosylated peptide sequence to the N-terminal end of non-glycosylated peptide sequence. Miller on the other hand teaches chemical ligation of an Asn-glycosylated peptide sequence to the C-terminal end of non-glycosylated peptide sequence. One of ordinary skill in the art would expect that both peptide sequences can be glycosylated and chemically ligated, since both N- and C-terminal peptide sequences having glycosylation can be chemically ligated independently.

Conclusion

22. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/J. H./
Examiner, Art Unit 1654

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Primary Examiner, Art Unit 1654